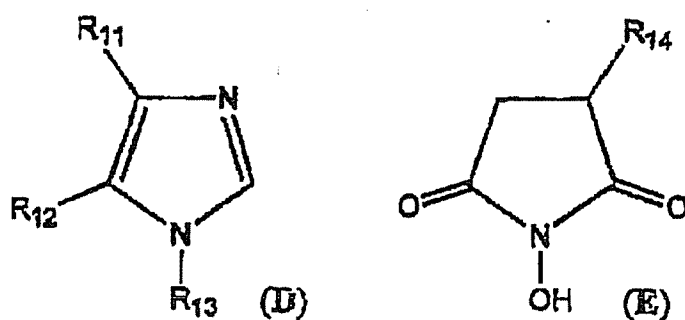


IN THE CLAIMS

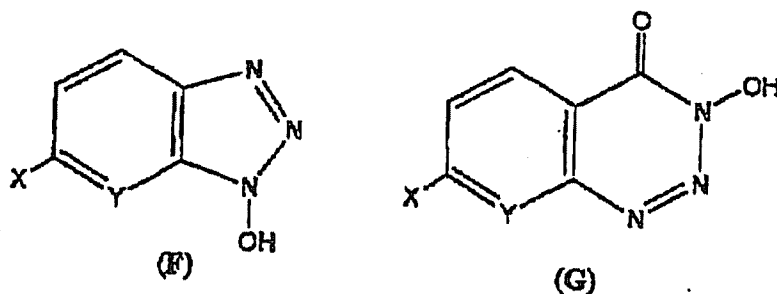
1. (Cancelled)
2. (Currently Amended) A method according to claim 7 in which the coupling agent is 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC).
3. (Original) A method according to claim 2, in which the coupling agent is the hydrochloride salt of EDC.
4. (Currently Amended) A method according to claim 7, in which the coupling enhancer is selected from the group consisting of:

A) a heterocyclic ring of formula (D) or formula (E),



wherein R<sub>11</sub> and R<sub>12</sub> can be the same or different, and each represent a hydrogen atom or a cyano group; R<sub>13</sub> represent a hydrogen atom or an alkyl group; and R<sub>14</sub> represent a hydrogen atom or a salt of a sulfonic acid; and

B) an unsaturated ~~5-6 membered~~ heterocyclic ring of formula (F) or formula (G),



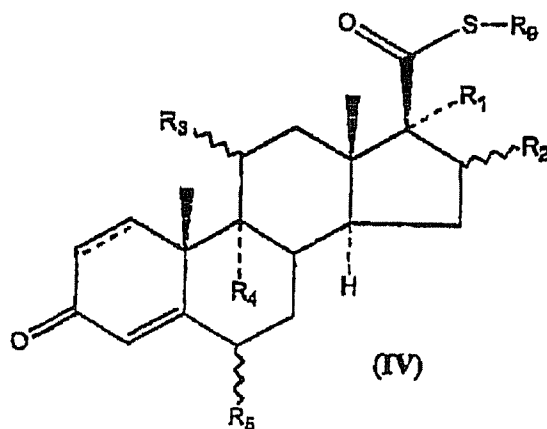
$X = H, F, Cl, Br$  and  $Y = CH, N, O, S$

5. (Currently Amended) A method according to claim 74, where the nucleophilic agent comprising a sulfur atom is selected from the group consisting of:

compounds of formula  $[M]^+ [SH]^-$  wherein M is a metal selected from ~~such as~~ Li, Na or K; or  $[M]^{2+} [S]^{2-}$  wherein M is a metal selected from ~~such as~~ Ca or Mg, the said sulfide salts being optionally hydrated; and an *in situ* generated sulfide salt or a hydrated sulfide salt.

6. (Currently Amended) The method of claim 74, wherein the nucleophilic agent is dissolved in a suitable solvent prior to addition to the reaction mixture, or wherein the nucleophilic agent is added in the form of a solid salt or as a solution of the salt in water, an organic solvent, or a combination thereof.

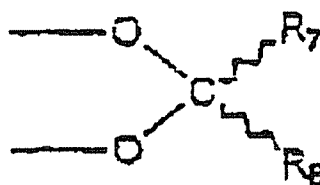
7. (Currently Amended) A method ~~according to claim 1~~ for preparing a steroidal carbothioic acid of formula (IV) or a salt thereof



wherein the symbol  $\equiv$  in the 1,2-position represent a single or a carbon-carbon double bond;

$R_1$  represents a hydrogen atom, a hydroxy- or an alkoxy group in the  $\alpha$ -configuration, a group  $-O-C(=O)-R_6$  wherein  $R_6$  is an alkyl group or an optionally substituted 5-6 membered heterocyclic ring containing either oxygen, nitrogen or sulfur as ring hetero atom;

$R_2$  represents a hydrogen atom, a hydroxy group, an alkoxy group in the  $n$ -configuration, an alkyl group which may be in either the  $\eta$ - or  $\beta$ -configuration, an alkylene group, wherein the alkylene group is bound to the steroid nucleus via a double bond, or  $R_1$  and  $R_2$  together represent



where  $R_7$  and  $R_8$  are the same or different and each represent a hydrogen atom or an alkyl group;

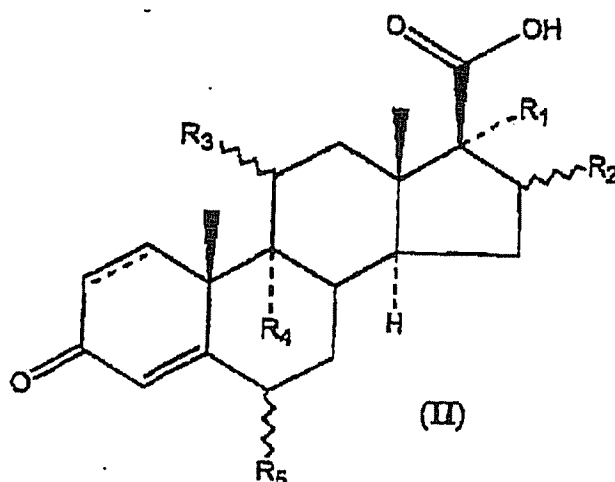
$R_3$  represent a hydrogen atom, hydroxy- or a protected hydroxy group in either a  $\alpha$ - or  $\beta$ -configuration or an oxo group;

$R_4$  represents a hydrogen- or a halogen atom or  $R_3$  and  $R_4$  together represent a carbon-carbon bond or an epoxy group in the  $\beta$ -configuration; and

$R_5$  represents a hydrogen- or a halogen atom in either the  $\alpha$ - or  $\beta$ -configuration;

$R_9$  represents a hydrogen atom or  $R_9$  represent a metal ion; the method comprising;

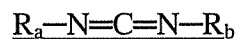
A) reacting a steroidal carboxylic acid of formula (II) or a salt thereof



in which the substituents of formula (II) have the above defined meaning with a coupling agent alone or in conjunction with an coupling enhancer, followed by the reaction with a nucleophilic agent comprising a sulfur atom; and optionally

B) reacting the product from step A) with an acid

wherein the coupling agent is selected from the group consisting of carbodiimide derivatives represented by the following formula:



wherein  $R_a$  and  $R_b$  are the same or different, and each represent an aliphatic, heteroaliphatic, carbocyclic or a heterocyclic group, wherein the group is optionally

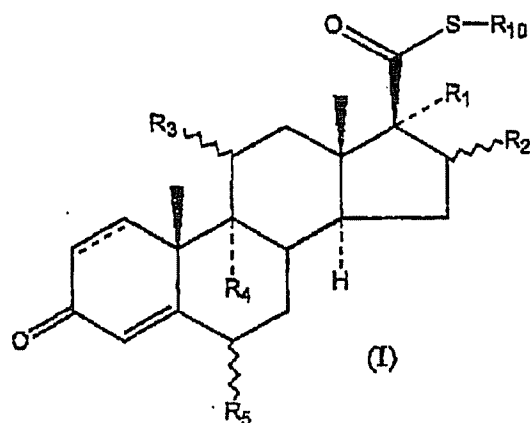
substituted.

8. (Currently Amended) The method of claim 71, wherein i)  
the coupling agent is added before the coupling enhancer, or  
the coupling enhancer is added before the coupling agent, and/or wherein ii)  
the steroidal carboxylic acid is added to a mixture of the coupling agent and the coupling  
enhancer, or wherein  
a mixture of the coupling agent and the coupling enhancer is added to a steroidal  
carboxylic acid, or wherein  
the steroidal carboxylic acid is added to a mixture of the coupling agent and the coupling  
enhancer in a polar aprotic solvent, ~~preferably DMF or DMA~~, at elevated temperature.

9. (Withdrawn) The method of claim 1, further comprising,  
reacting the steroidal carbothioic acid or a salt thereof with an electrophilic agent to  
produce a steroidal carbothioate, or a salt thereof.

10. (Withdrawn) A method according to claim 9, in which the electrophilic agent is  
selected from the group consisting of: C<sub>1-8</sub> di- or trihaloalkanes.

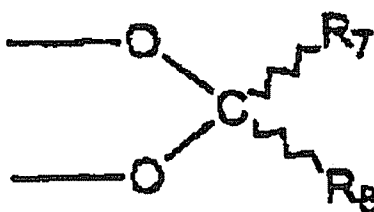
11. (Withdrawn) A method according to claim 9 for preparing a steroidal carbothioate of  
formula (I)



wherein  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$  and  $R_5$  are;

$R_1$  represents a hydrogen atom, a hydroxy- or an alkoxy group in the  $\alpha$ -configuration, a group  $-O-C(=O)-R_6$  is an alkyl group or an optionally substituted 5-6 membered heterocyclic ring containing either oxygen, nitrogen or sulfur as ring hetero atom;

$R_2$  represents a hydrogen atom, a hydroxy group, an alkoxy group in the  $n$ -configuration, an alkyl group which may be in either the  $\eta$ - or  $\beta$ -configuration, an alkylene group, wherein the alkylene group is bound to the steroid nucleus via a double bond, or  $R_1$  and  $R_2$  together represent



where  $R_7$  and  $R_8$  are the same or different and each represent a hydrogen atom or an alkyl group;

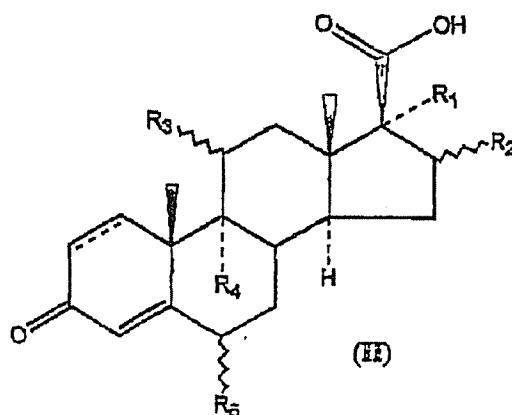
$R_3$  represent a hydrogen atom, hydroxy-or a protected hydroxy group in either a  $\alpha$ - or  $\beta$ -configuration or an oxo group;

$R_4$  represents a hydrogen- or a halogen atom or  $R_3$  and  $R_4$  together represent a carbon-carbon bond or an epoxy group in the  $\beta$ -configuration; and

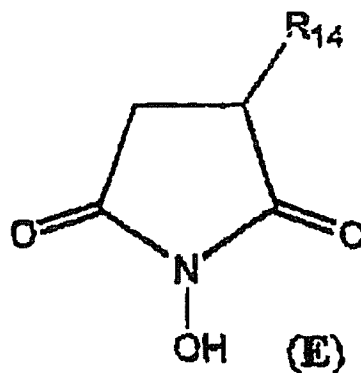
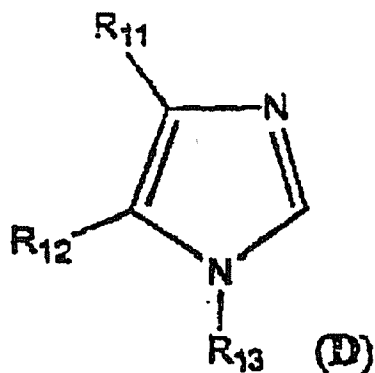
$R_5$  represents a hydrogen- or a halogen atom in either the  $\alpha$ - or  $\beta$ -configuration

and  $R_{10}$  represents a  $C_{15}$  haloalkyl or an optionally substituted heterocyclic ring, the method comprising:

A) reacting a steroidal carboxylic acid of formula (II)



with a coupling agent and a coupling enhancer of formula (D) or formula(E)]



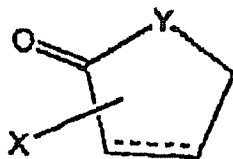
wherein  $R_{11}$  and  $R_{12}$  independently represent a hydrogen atom or a cyano group ( $C\equiv N$ );

$R_{12}$  represent a hydrogen atom or an alkyl group; and

$R_{14}$  represent a hydrogen atom or a moiety of a sulfonic acid

B) reacting the product from step A) with a nucleophilic agent comprising sulfur; and

C) reacting the product from step B) with an electrophilic agent or a compound of the following formula;



wherein  $X=H, F, Cl, \text{ or } Br$  and;  $Y=CH_2, NH, O, \text{ or } S$ .

12. (Withdrawn) The method of claim 11, wherein the coupling enhancer is selected from the group consisting of: NMI (N-methylimidazole); DCI (4,5-dicyanolmidazole); NHS (N-hydroxysuccinimide); and sulfo-NHS (N-hydroxysulfosuccinimide).

13. (Withdrawn) The method of claim 11, wherein step C) constitutes the *in situ* reaction of the product from step B) with bromofluoromethane to form a compound of formula (I) wherein  $R_{10}$  is a fluoromethyl group.

14. (Withdrawn) The method according to claim 9, in which at least two subsequent steps are performed *in situ*;



the method is conducted as a continuous method;  
step A), B) and optionally step C) are conducted as a one-pot synthesis without solvent changes. are performed at room or elevated temperature, or both; or  
a combination of one or more of the foregoing.

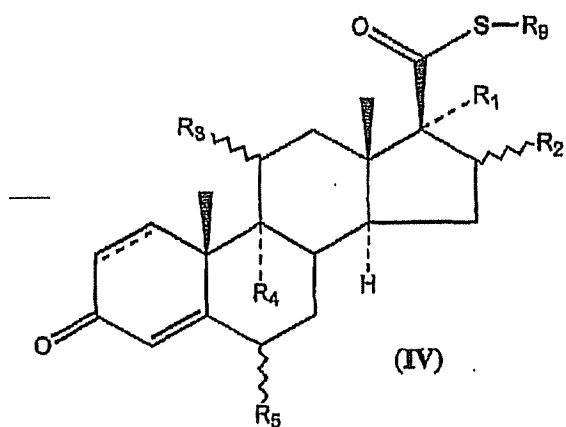
15. (Withdrawn) The method of claim 9, wherein an androstane 17 $\beta$ -carboxylic acid is converted to an androstane 17 $\beta$ -carbothioate.

16. (Withdrawn) The method of claim 9, wherein step B) provides a compound of formula (IV), in which the moiety  $-5-R_5$  represent a group of the formula  $[-S][M]^+$  wherein M is a metal such as Li, Na or K,

wherein the symbol  $\equiv$  in the 1,2-position represent a single or a carbon-carbon double bond;

$R_1$  represents a hydrogen atom, a hydroxy- or an alkoxy group in the  $\alpha$ -configuration, a group  $-O-C(=O)-R_6$  is an alkyl group or an optionally substituted 5-6 membered heterocyclic ring containing either oxygen, nitrogen or sulfur as ring hetero atom;

$R_2$  represents a hydrogen atom, a hydroxy group, an alkoxy group in the  $n$ -configuration, an alkyl group which may be in either the  $\eta$ - or  $\beta$ -configuration, an alkylene group, wherein the alkylene group is bound to the steroid nucleus via a double bond, or  $R_1$  and  $R_2$  together represent



where  $R_7$  and  $R_8$  are the same or different and each represent a hydrogen atom or an alkyl group;

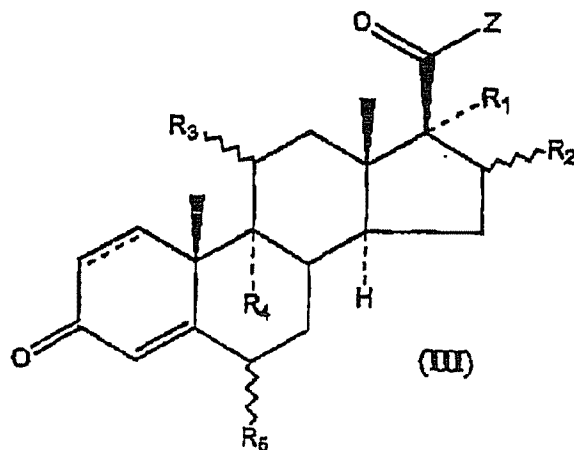
$R_3$  represent a hydrogen atom, hydroxy-or a protected hydroxy group in either a  $\alpha$ - or  $\beta$ -configuration or an oxo group;

$R_4$  represents a hydrogen- or a halogen atom or  $R_3$  and  $R_4$  together represent a carbon-carbon bond or an epoxy group in the  $\beta$ -configuration; and

$R_5$  represents a hydrogen- or a halogen atom in either the  $\alpha$ - or  $\beta$ -configuration;

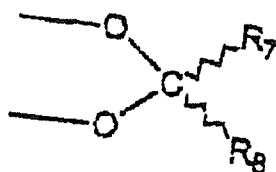
$R_9$  represents a hydrogen atom or  $R_9$  represent a metal ion.

17. (Withdrawn) A compound of the formula (III) and salts and solvates thereof



wherein  $R_1$  represents a hydrogen atom, a hydroxy- or an alkoxy group in the  $\alpha$ -configuration, a group  $-O-C(=O)-R_6$  is an alkyl group or an optionally substituted 5-6 membered heterocyclic ring containing either oxygen, nitrogen or sulfur as ring hetero atom;

$R_2$  represents a hydrogen atom, a hydroxy group, an alkoxy group in the  $n$ -configuration, an alkyl group which may be in either the  $\eta$ - or  $\beta$ -configuration, an alkylene group, wherein the alkylene group is bound to the steroid nucleus via a double bond, or  $R_1$  and  $R_2$  together represent



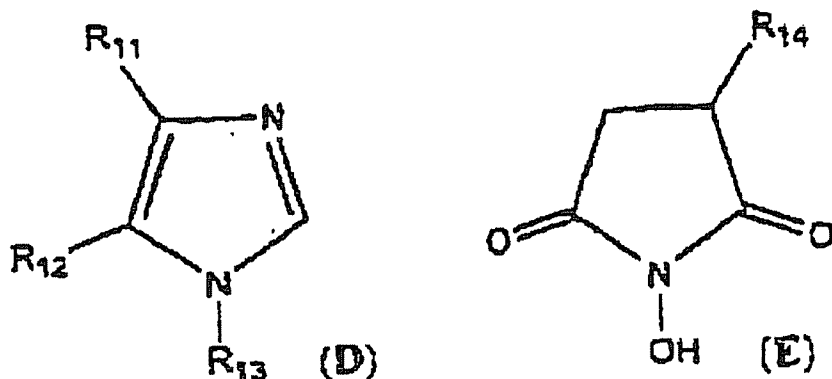
where  $R_7$  and  $R_8$  are the same or different and each represent a hydrogen atom or an alkyl group;

$R_3$  represent a hydrogen atom, hydroxy- or a protected hydroxy group in either a  $\alpha$ - or  $\beta$ -configuration or an oxo group;

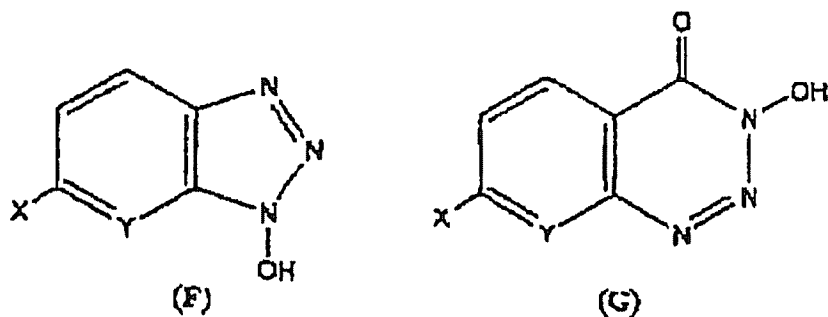
$R_4$  represents a hydrogen- or a halogen atom or  $R_3$  and  $R_4$  together represent a carbon-carbon bond or an epoxy group in the  $\beta$ -configuration; and

$R_5$  represents a hydrogen- or a halogen atom in either the  $\alpha$ - or  $\beta$ -configuration; and

Z represent the structural moiety resulting from the reaction between the steroidal carboxylic acid of formula (II) and a coupling agent, followed by a coupling enhancer selected from the group consisting of the compounds of formulas (D); (E); (F); and (G):



wherein  $R_{11}$  and  $R_{12}$  independently represent a hydrogen atom or a cyano group;  $R_{13}$  represent a hydrogen atom or a methyl group; and  $R_{14}$  represent a hydrogen atom or a moiety of a sulfonic acid,



X - H, F, Cl, Br and Y - CH, N, O, S

with the proviso that:

when the coupling enhancer is a compound of formula (F), X can not represent H when Y represents CH:

when the coupling enhancer is a compound of formula (D),  $R_{11}$  and  $R_{12}$  can not both represent H when  $R_1$  in formula III represents DH; and

when the coupling enhancer is a compound of formula (E),  $R_{14}$  can not represent H when  $R_1$  in formula III represents H;

and with the further proviso that

succinimidyl-9-fluoro-11 $\beta$ , 17 $\alpha$ -dihydroxy-16 $\alpha$ -methyl-3-oxoandrosta-1,4-diene-17 $\beta$ -carboxylate;

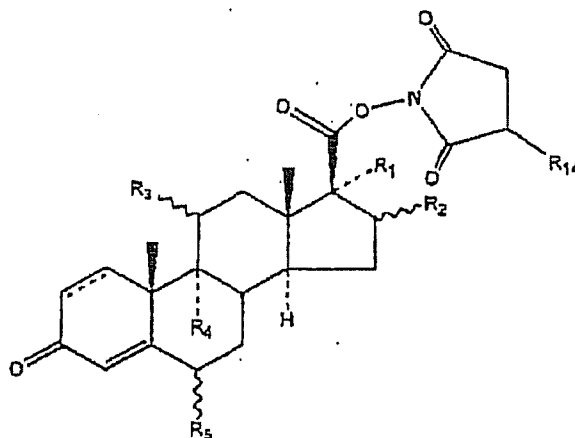
17 $\alpha$ -hydroxy-4-androsten-3-one-17 $\beta$ -carboxylic acid N-hydroxysuccinimide ester;

N-hydroxysuccinimidyl-9-fluoro-16 $\alpha$ -methyl-11 $\beta$ , 17-dihydroxy-3-oxo-1,4-androstadiene-17 $\beta$ -carboxyester;

N-hydroxysuccinimide ester of dexamethasone-17 $\beta$ -carboxylic acid; and 1-[(9-fluoro-11 $\beta$ -hydroxy-16 $\beta$ -methyl-3-oxo-17 $\alpha$ -propionylxyandrosta-1,4-dien-17 $\beta$ -yl)carbonyl]imidazole are disclaimed.

18. (Withdrawn) The compound of claim 17, wherein at least one of  $R_{11}$  and  $R_{12}$  is a cyano group ( $C\equiv N$ ),  $R_{13}$  is a hydrogen atom, formula (D) is NMI (N-methylimidazole) or DCI (4,5-dicyano-imidazole), formula (E) is NHS (N-hydroxysuccinimide) or sulfo-NHS (N-hydroxysulfosuccinimide), or a combination comprising one or more of the foregoing.

19. (Withdrawn) The compound of claim 17, having the formula:



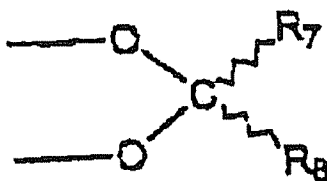
with the proviso that R<sub>14</sub> can not represent H when R<sub>1</sub> represents H.

20.( Withdrawn) A compound of the formula (VI) and salts and solvates thereof

wherein

R<sub>1</sub> represents a hydrogen atom, a hydroxy- or an alkoxy group in the  $\alpha$ -configuration, a group -O-C(=O)-R<sub>6</sub> is an alkyl group or an optionally substituted 5-6 membered heterocyclic ring containing either oxygen, nitrogen or sulfur as ring hetero atom;

R<sub>2</sub> represents a hydrogen atom, a hydroxy group, an alkoxy group in the  $n$ -configuration, an alkyl group which may be in either the  $\eta$ - or  $\beta$ -configuration, an alkylene group, wherein the alkylene group is bound to the steroid nucleus via a double bond, or R<sub>1</sub> and R<sub>2</sub> together represent



where R<sub>7</sub> and R<sub>8</sub> are the same or different and each represent a hydrogen atom or an alkyl group;

$R_3$  represent a hydrogen atom, hydroxy-or a protected hydroxy group in either a  $\alpha$ - or  $\beta$ -configuration or an oxo group;

$R_4$  represents a hydrogen- or a halogen atom or  $R_3$  and  $R_4$  together represent a carbon-carbon bond or an epoxy group in the  $\beta$ -configuration; and

$R_5$  represents a hydrogen- or a halogen atom in either the  $\alpha$ - or  $\beta$ -configuration, wherein  $R_a$  and  $R_b$  are the same or different, and each represent an aliphatic, heteroaliphatic, carbocyclic or a heterocyclic group;

with the proviso that 1-(3-dimethylamino-propyl)-3-ethyl-carbodiimide-6 $\alpha$ , 9 $\nu$ -difluoro-11 $\beta$ -hydroxy-16 $\alpha$ , 17 $\alpha$ -isopropylidenedioxy-3-oxo-androsta-1,4-diene-17 $\beta$ -carboxylate is disclaimed.

21-23. (Cancelled).

24. (New) The method of claim 8, wherein the polar aprotic solvent is DMF or DMA.